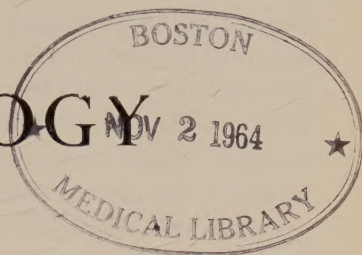


# THE BRITISH JOURNAL OF DERMATOLOGY

JULY 1960



THE BRITISH ASSOCIATION OF DERMATOLOGY

SIR ARCHIBALD GRAY.

It has been suggested that I should write a short history of the British Association of Dermatology. I find this somewhat embarrassing as I was intimately concerned with its inception and cannot entirely avoid the personal element. At the same time this seems an appropriate moment to look back to the birth of the Association as this year it completes the fortieth of its existence.

I shall not in this short article attempt to deal with the scientific side of the Association's work. This can be found in various numbers of the British Journal of Dermatology. It will suffice to say that the papers read at the meetings have been of a very high standard and the Association has been fortunate in having a large number of distinguished visitors from at home and abroad to address it on numerous occasions.

As the Association really derived from the British Journal of Dermatology, it is necessary to begin with a note about the early history of the Journal. The Journal first appeared in 1888 under the Editorship of Mr. Malcolm Morris and Dr. H. G. Brooke. It would appear that these two gentlemen owned the Journal and made themselves responsible for the cost of its publication.

In March 1891 a meeting was called of a few leading dermatologists to consider the future of the Journal, as the accounts showed that at the end of 1890 the loss amounted to about £100. This meeting resolved:

"That the following gentlemen constitute a syndicate to manage and finance the British Journal of Dermatology formally handed over to them by Dr. H. G. Brooke and Mr. Malcolm Morris; viz. Dr. H. G. Brooke, Dr. Radcliffe Crocker, Dr. Colcott Fox, Mr. Malcolm Morris, Dr. J. F. Payne, and Dr. J. J. Pringle".

It was also agreed to form an Editorial Committee with Mr. Malcolm Morris as Chairman and Dr. Pringle as Secretary and Acting Editor.

In 1894 some complicated arrangements were made by which the Dermatological Society of Great Britain and Ireland made an annual contribution to

the cost of the Journal and in 1896 the Dermatological Society of London also agreed to contribute but, in spite of this, the annual loss continued and members of the Editorial Committee were contributing annually sums up to as much as £15 to meet these deficits. This was felt to be rather a strain and in 1898 a further thirteen dermatologists agreed to guarantee sums up to £10 per annum. These gentlemen were described as cooperating members but had no say in the control of the Journal.

Up till 1896 no regular annual accounts were produced but on and after that date, when Dr. Galloway succeeded Dr. Pringle as Editor, regular annual accounts were published and for the eleven years from 1896–1906 the total losses on the Journal amounted to approximately £1000 which was made good by contributions from the Editorial Committee and cooperating members.

In 1907, during the Editorship of Dr. Macleod who had succeeded Dr. Galloway in 1905, another crisis occurred. The Royal Society of Medicine was founded and the two dermatological societies mentioned above were merged into the Dermatological Section of that Society. As it was clear that the R.S.M. would not contribute to the Journal nor take it over, this entailed an annual loss of some £50 a year. In November 1907 a meeting of dermatologists was called to invite all interested to become guarantors of sums up to £3 to meet any deficits which might arise in future. Some thirty dermatologists agreed to become guarantors. At a meeting held in February 1908 it was decided that the management of the Journal should pass to the guarantors who would annually elect an Editor and an Editorial Committee. At this meeting Dr. MacLeod was re-elected Editor and at the first meeting of the Editorial Committee Mr. Malcolm Morris was elected its Chairman, a post which he had held in the old Editorial Committee since its formation in 1891.

Under this management the Journal continued to be produced but it had already become self-supporting, for from 1907 up to the present day there was only one year in which there was a small deficit, which was absorbed in the following year, so that the new guarantors were never called upon. The only change of importance that occurred during this period was the change of name to the British Journal of Dermatology and Syphilis, which was agreed at the Annual Meeting in March 1917.

Dr. MacLeod resigned his Editorship at the end of 1910 and was succeeded by Dr. Sequeira, who in turn retired at the end of 1915 and I was appointed in his place. During the 1914–18 War I had to visit all the Universities in Great Britain and I took the opportunity to call on some of the local dermatologists who gave me the impression that they were rather ignored by their London colleagues. It seemed that the physicians had solved this problem by founding the Association of Physicians, which met periodically in the provinces.

Nothing could be done till the War was over but at a meeting held on 28th July 1919 the following appears in the minutes of the Editorial Committee :



"The Editor brought forward a suggestion that the guarantors should form themselves into an Association for the purpose of conducting the Journal and also for holding an annual congress, alternately in London and in a provincial centre, with the object of (i) promoting a free interchange of views between the London and provincial dermatologists and (ii) dealing more with the academic side of dermatology and syphilis than was possible at the ordinary clinical meetings of the Dermatological Section of the Royal Society of Medicine".

This suggestion was referred to a sub-committee who reported :

"It has been proposed that an Association of British Dermatologists should be formed with the following objects :—

(i) To hold an annual meeting, alternately in London and in a provincial centre, lasting one to three days at which subjects of interest in dermatology and syphilology should be discussed. (ii) To become the proprietors of this Journal, at present owned by a number of guarantors.

Such Association would in no way interfere with the work of existing dermatological societies but would have the advantage (i) of bringing together London and provincial dermatologists at more regular intervals than has been possible in the past ; (ii) of dealing with the academic side of dermatology and syphilology in a way that is not possible in existing dermatological societies, which are mainly clinical in type ; (iii) of stimulating investigation into dermatological problems ; and (iv) of increasing interest in and obtaining more material for publication in the Journal, which is the sole organ of British dermatology and at present compares unfavourably with many foreign publications.

It is suggested that, in order to confine the Association to pure dermatologists, the number should be strictly limited : the number proposed being one hundred. Membership might consist of Ordinary members, Colonial members (who would probably have to form a separate class, as it would not be possible to ask for the same contribution from them as from members in the British Isles, but their membership would be much desired) and Corresponding members (who would be foreigners of distinction in the dermatological world).

The Association should be administered by a Council and the President for the year would be chosen from the centre in which the annual meeting would be held. One or more local secretaries would have to be selected and a permanent secretary in London would probably be necessary".

The Editorial Committee agreed unanimously to approve the formation of a Dermatological Association on the lines indicated and agreed to circulate the memorandum to the guarantors.

At a meeting of the guarantors held on 18th December 1919 the following resolution was passed :

"(i) That the meeting of guarantors approves of the scheme for the formation of an Association of Dermatology submitted by the Editorial Committee.

(ii) That the name of the Association shall be the British Association of Dermatology and Syphilology.

(iii) That the Editorial Committee be instructed to draw up detailed regulations for the Association on the basis of their memorandum and that copies of these be circulated to the guarantors of the Journal.

(iv) That those guarantors who signify their desire to become members of the Association shall *ipso facto* be the first members of the Association".

In pursuance of the above resolution, the Editorial Committee set up a sub-committee to draft Rules for the proposed Association. These were approved by the Editorial Committee, with certain modifications, in May 1921 and by the guarantors in June of the same year. At this latter meeting it was also agreed to arrange for the first meeting of the Association to be held in London in November 1921 and that the Editorial Committee should act as the Executive Committee until this meeting. Sir Malcolm Morris was elected President and the Editor Acting Secretary, while Dr. Barber was appointed Local Secretary for the meeting.

The first Meeting duly took place at the Royal Society of Medicine on 18th November 1921 and at that meeting the new Rules were first brought into force and an Executive Committee was appointed. It was also agreed to hold the second Annual Meeting in Edinburgh with Dr. Norman Walker as President, Dr. Pringle as Treasurer and Dr. Whitfield as Secretary. The Editor was reappointed. From then onwards, Annual Meetings have been held every year, though on two occasions, in 1944 owing to travel difficulties during the War, and in 1952 owing to the International Congress being held in London, only business meetings were held.

The Rules adopted in 1921 still form the basis of those at present in force but some alterations have been made in the intervening years. In 1950 it was decided to drop the words "and Syphilology" from the title of the Association and at the same time the words "and Syphilis" were removed from the title of the Journal. In 1927 a new group of "Honorary Members" was introduced and in 1953 "Corresponding Members" became "Honorary Foreign Members".

There has always been some difference of opinion as to the limitation of membership, some feeling that such limitation enables the Association to maintain a high standard, while others think that it prevents many of the younger dermatologists from obtaining the advantages which membership provides. There has been a very considerable increase in highly trained dermatologists especially since the introduction of the National Health Service in 1948. The attendance at the early meetings of the Association numbered about 30 but in the last few years it has been in the neighbourhood of 150. At present the view is that, although some limit should be retained, it should be raised. Therefore in 1950 the number was increased to 120 and in 1958 to 130. It is proposed this year to increase it to 150. In addition to this it was agreed in 1956 to place all Ordinary Members over sixty-five years of age in a special group called "Senior Ordinary Members" who should not be reckoned when calculating vacancies.

No special provision was made in the original Rules for Overseas Members although there were two Commonwealth members in the first list. At the Executive Committee Meeting in December 1926 it was suggested that Branches



of the Association should be formed in Canada and Australia, which should be governed by the Rules of the Association, but would be autonomous in so far as the election of their members was concerned. Letters were written to representatives of the Canadian and Australian dermatologists and at the Annual Meeting in 1927 the Canadian and New South Wales Branches were incorporated. The Melbourne Branch was admitted the following year. Since then Branches have been established in West Australia (1948), New Zealand (1954), Queensland (1955) and South Australia (1956). The subscription of members of the Overseas Branches has been limited to the subscription to the Journal, which all members receive, and it was left to the Branches to add any sums they required for administrative purposes.

Although not laid down in the Rules, it has been the custom to appoint the President from the place where the Annual Meeting was held. It was also felt that the Secretary should be resident in London and so the member who was likely to be the next President when the Annual Meeting was to be held in London was appointed Secretary. He would normally hold office for three years. The whole matter was discussed in 1955 when it was agreed that in future the President should be chosen annually irrespective of his place of residence. It was also proposed that a Vice-President should also be appointed annually and if the Meeting was held at a place which was not the President's residence, the Vice-President should be one of the local dermatologists. In these changed circumstances the post of Secretary was left quite open and no limit was placed on the holding of this office, subject to annual re-election.

A few years after the War, the Secretary-General of the Permanent International Dermatological Committee, Dr. Lomholt, was anxious that another International Congress should be held, the last having been in Budapest in 1935, and he made strong representations to the Association that the next Congress should be held in London. The Association, after much thought, agreed to arrange this. Various committees were set up and eventually the Xth International Congress of Dermatology was held at Bedford College in July 1952. Thanks to the untiring efforts of the committees and their officers the Congress was entirely successful.

The Association has from time to time appointed committees to discuss the place of dermatology in both undergraduate and postgraduate education. It gave evidence before the Interdepartmental (Goodenough) Committee on Medical Education and has recently given evidence before a Working Party set up by the Minister of Health and the Secretary of State for Scotland to consider the staffing of hospitals. In 1943 an agreement was reached with the Council of the Faculty of Radiologists laying down general principles which should guide the relationship between the two branches of the profession.

At the Annual Meeting in 1934 it was suggested that a fund should be raised to commemorate the life and work of Robert Willan. It was proposed that

such a fund should be used to place a tablet in the church in Madeira, where he is buried and to award a medal, at agreed intervals, to some British dermatologist who had made distinguished contributions to dermatology. Just before the War, when some funds had become available, designs for a tablet were considered but it then became clear that there was nowhere in Madeira which was suitable for placing such a tablet. The matter was therefore left in abeyance for the time being. During the War the Association received a very generous gift of £25 from the Canadian Branch and after the War, as this sum had not been used, the Branch was asked if this sum might be added to the Willan Fund. At the end of the International Congress in 1952 some balance was left in the hands of the Association and it was decided to add this to the Willan Fund.

Knowing that the Royal College of Physicians was about to rebuild, it was decided that it would be an excellent memorial to Willan if the College would be prepared to name one of its rooms the "Willan Room" which should house the works of Willan, including the original drawings of his Atlas, which the College possesses, together with other important dermatological works. The Royal College has kindly agreed to this proposition and is planning to establish such a room in its new building. This should also encourage a closer liaison between general medicine and one of its more important specialities.

I have tried to give an outline of the foundation of the Association and some of its work, apart from its clinical and scientific activity, which would take a volume in itself. There can be no doubt, however, that the Association has been a vital factor in maintaining the high standard for which British Dermatology had already been well known. The success of the Association has depended on the willing co-operation of British dermatologists since its inception and I cannot end without paying a special tribute to Sir Malcolm Morris, who founded the Journal, and nursed it through its teething years. As Chairman of the Editorial Committee, he presided over the birth of the Association and was its first President.

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# THE ACTION SPECTRUM OF 8-METHOXYPSORALEN FOR ERYTHEMA IN HUMAN SKIN.

## PRELIMINARY STUDIES WITH A MONOCHROMATOR.

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As shown by a recent issue of the *Journal of Investigative Dermatology*, 32 (1959), interest has steadily increased in the furocoumarins and their capacity for augmenting the sensitivity of skin to sunlight since clinical trials of these substances were first reported by El Mofty (1948) and later by Sidi and Bourgeois-Garvardin (1952) and Lerner, Denton and Fitzpatrick (1953).

The furocoumarin which has been chiefly used by dermatologists is xanthotoxin, or 8-methoxypsoralen (8-MOP). So far as we know, however, its action spectrum and that of other furocoumarins for photosensitizing skin has not been determined, though various observations suggest that it lies in the longer wavelengths of the ultra-violet region. For instance, Stegmaier (1959) observed in persons taking 8-MOP orally that erythema developed after exposure to fluorescent lamps which emitted most of their energy at 320–360  $m\mu$ . Previously, Kuske (1940) had shown that furocoumarins applied locally to the skin led to photosensitization to the 334 and 366  $m\mu$  lines of the mercury arc spectrum from a monochromator. Evidently the action spectrum of 8-MOP lies above 320  $m\mu$  and is quite different from that which causes normal sunburn (280–320  $m\mu$ ). This paper describes some preliminary work attempting to clarify the matter.

## MATERIALS AND METHODS.

The source of radiant energy was a 2 KW high-pressure xenon arc chosen for use with a monochromator which has been described elsewhere (Magnus, Porter, McCree, Moreland and Wright, 1959). The spectral emission of this arc extends continuously from about 250 to 1400  $m\mu$ . As well as using the monochromator, radiation was collected from the arc by two quartz lenses and focused directly on to the skin so that an intense beam of energy of broad spectrum was available for preliminary experiments.

I. (i) The first tests were made on skin which had been painted  $1\frac{1}{2}$  hours previously with a 1% solution of 8-MOP (Light and Co.) in chloroform. An area 2 cm. in diameter was irradiated for 5 minutes, with a glass spectrophotometric cuvette filled with distilled water intervening (optical depth 3 cm.), so as to cut out the "sunburn spectrum" and reduce the amount of infra-red rays, the latter being liable to produce intolerable burning during an exposure. The wavelengths thus transmitted ranged from about 320 to 1300  $m\mu$ .

(ii) Further pilot tests using the same spectrum, but with various filter combinations, were made on two persons who had ingested 20 mg. of 8-MOP (Upjohn and Co.)  $1\frac{1}{2}$  hours previously. The filters were plate glass and Chance Glass OY18 and

OX7. Again water was used as an additional filter, this time in a quartz cuvette (3 cm. optical depth) to reduce the intensity of the infra-red radiation.

II. (i) Using the monochromator on a male subject, forearm skin, which had been painted with a 1% solution of 8-MOP  $1\frac{1}{2}$  hours previously, was exposed to radiation of serially increasing duration and of narrow waveband at 10 m $\mu$  intervals between 250 and 450 m $\mu$ . The other forearm, painted with chloroform only, was similarly irradiated as a control. In each case the area of skin irradiated was approximately 2 by 4 mm. The object of this procedure was to find the limits of the action spectrum and the order of the duration of exposures required for the determination of the minimal erythematous dose (MED).

(ii) This procedure was next used on the skin of the back. Three ml. of a 1% solution of 8-MOP in chloroform were applied to an area of about 30 square cm. A similar control area was treated with chloroform only, and both irradiated  $1\frac{1}{2}$  to 2 hours later with the monochromator. Multiple exposures were made lasting from a few seconds to 1 hour, depending on the wavelength used, at intervals of 10 m $\mu$  in the range 250–420 m $\mu$ . The subjects used were three men of average skin colour, aged 26, 38 and 62 years. Test sites were examined at regular intervals, usually every 3 to 4 hours for the first 16 hours, and subsequently at longer intervals, for at least 4 days.

(iii) Lastly, similar MED tests with the monochromator were made on four other persons who had swallowed 20 mg. of 8-MOP  $1\frac{1}{2}$  hours previous to irradiation. Only one subject, a woman aged 28 of European stock and slightly darker skin colour than average, was tested to a fairly wide spectral range. Three other male subjects were tested in some parts of the long ultra-violet spectrum, but for various reasons their tests were not continued.

## RESULTS.

I. With radiation of wide spectrum. (i) Forearm skin painted with 8-MOP and irradiated through plate glass and water for 5 minutes in two subjects gave rise to strong immediate and persistent erythema, followed about  $\frac{1}{2}$ –1 hour later by the development of a blister. (ii) Irradiation through certain filter combinations of the skin of the anterior abdomen of two subjects who had taken 8-MOP orally gave results suggesting that the action spectrum lay between 320 and 400 m $\mu$ , for without 8-MOP, erythema only developed with Chance Glass OX7 (transmitting about 250 to 400 m $\mu$  plus some red and infra-red) or with no filter at all. However, after 8-MOP, erythema developed also on sites irradiated through plate glass (transmitting about 320 m $\mu$  upwards) but not through Chance Glass OY18 (transmitting about 400 m $\mu$  upwards).

II. With radiation of narrow waveband. (i) Forearm skin was painted with 8-MOP and irradiated between 250 and 450 m $\mu$ . From 320 to 350 m $\mu$ , with exposures of 1 to 5 minutes, strong erythema resulted, usually after a latent period of up to 24 hours, followed by a blister 2 to 3 days later. Where an exposure was near the MED, erythema took longer to develop, i.e. about 48 hours and no blister followed. From 360 to 380 m $\mu$ , only erythema was seen and no blister. Subsequent pigmentation was roughly proportional to the intensity of the preceding erythema, and took a varying time to appear, usually 5 to 7 days (Fig. 1). On the control forearm, exposures at wave-



lengths above 330  $m\mu$  failed to produce any erythema with the exposures used (up to 30 minutes). Owing to the well known variation of susceptibility of the skin on different parts of the forearm to ultra-violet radiation, this pilot experiment is probably not of great reliability. (ii) In the determination of the MED at different wavelengths on the skin of the back, after being painted with 8-MOP, the following behaviour of the erythematous responses was noted. In the long ultra-violet, the MED on skin treated with 8-MOP did not usually result in any persistent erythema for as long as 48 hours after exposure. On

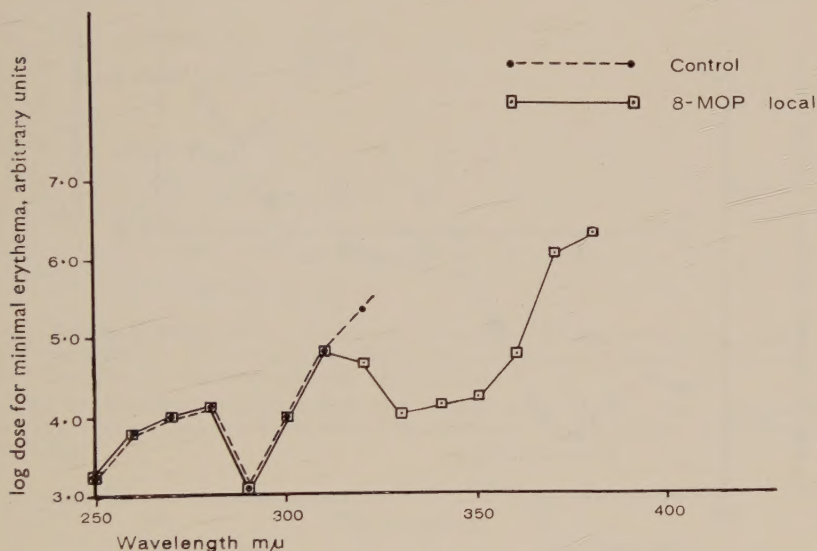


FIG. 1.—Result of MED tests at various wavelengths on forearm skin with and without local 8-MOP. No response on control skin at wavelengths above 320  $m\mu$ . 8-MOP treated skin produced erythema up to 380  $m\mu$ .

untreated skin, however, exposure in this spectral region often led to immediate erythema which persisted, or faded slightly to become more obvious 6 to 18 hours later. In untreated skin, the MED in the long-ultra-violet was much higher than that required in skin treated with 8-MOP, whereas below 320  $m\mu$  no very significant difference could be seen, except occasionally where untreated skin seemed slightly more sensitive than that treated with 8-MOP, suggesting that the psoralen was acting as a light filter. The results were plotted as graphs, of which Fig. 2 is an example. The graphs of the three subjects did not show any gross differences and all gave the same result for the extent of the action spectrum of 8-MOP, namely 320 to 370  $m\mu$ . They also showed that for 8-MOP to be effective, the least energy required was at 320  $m\mu$ . (iii) Determinations of MED at various wavelengths in persons who had ingested 8-MOP were unsatisfactory. Bullous and erythematous reactions

were obtained in two subjects from exposures at 320 and 330  $m\mu$  with doses that normally were without effect. Only erythematous reactions were obtained in another two at these wavelengths, but responses in general were not reproducible, being often feeble or negative in most cases at 350  $m\mu$  and above. However, the results obtained in one subject, in whom the tests were more informative and were made over a fairly wide spectral range are shown in Fig. 3. Unfortunately, this subject reacted to long ultra-violet under normal conditions, i.e. when *not* taking 8-MOP, by producing immediate pigmentation,

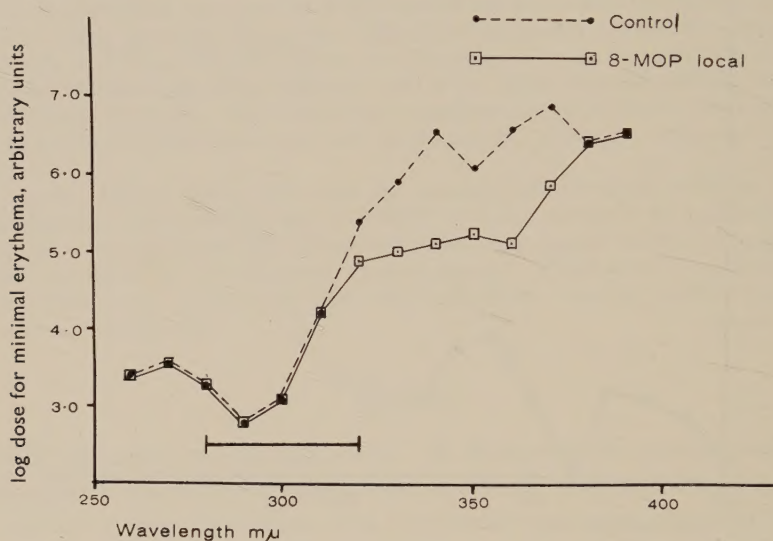


FIG. 2.—Example of results in a subject of MED tests at various wavelengths on the skin of the back, with and without local 8-MOP.

The horizontal line extending from 280–320  $m\mu$  and lying below the curve indicates the approximate limits of the waveband that produces normal erythema from exposure to sunlight.

so-called “pigment darkening”; persistent erythematous responses were not obtained with wavelengths longer than 330  $m\mu$ , though occasionally a transient immediate erythematous response was seen.

In one test subject it was noted that the skin had become deeply sunburnt after he had worked in his garden for half an hour wearing a cotton shirt which entirely covered an area of skin painted with 8-MOP. A different area of covered skin was then painted and the man again worked in strong sunlight in his garden wearing a similar shirt, with the same result. Exposures were then made at 340 and 360  $m\mu$  on another subject on skin painted with 8-MOP with each shirt over the exit slit of the monochromator. Erythematous reactions were obtained through each cotton fabric with doses that caused blistering where the skin was not covered.



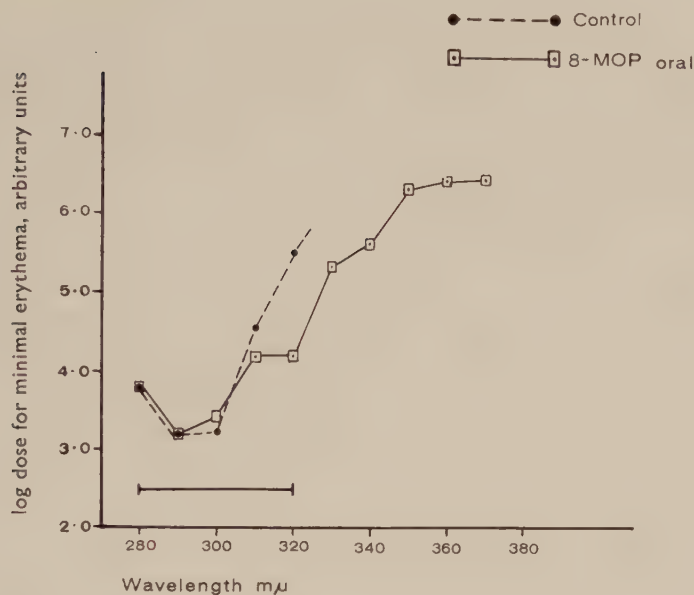


FIG. 3.—Results of MED tests at various wavelengths on the skin of the back, before and after oral 8-MOP. No persistent erythema in control tests at wavelengths above 320  $m\mu$ . Oral 8-MOP produced responses up to 370  $m\mu$ .

The horizontal line extending from 280–320  $m\mu$  and lying below the curve indicates the approximate limits of the waveband that produces normal erythema from exposure to sunlight.

### DISCUSSION.

The results described suggest that the action spectrum of 8-MOP, applied locally, lies between 320 and 370  $m\mu$ . This is in accord with the observations of Kuske (1940) and exactly corresponds with the limits of the action spectrum of oil of persian lime as found by Sams (1941).\*

Little is known of the mechanism whereby chemical substances augment the erythematous responses of skin to light, but 8-MOP seems to differ from sulphanilamide and chlorpromazine which, it has been suggested, merely enhance the normal sunburn reaction (Blum, 1941; Epstein, Brunsting, Petersen and Schwarz, 1957). That this is improbable with 8-MOP is indicated by the marked difference between its action spectrum (320–370  $m\mu$ ) and that of normal sunburn (280–320  $m\mu$ ). Since a photosensitizing substance can only act after absorbing energy, the action spectrum should correspond to the absorption spectrum. This would seem to apply to porphyrin (Magnus, Porter and Rimington, 1959), probably to chlorothiazide, (Harber, Lashinsky and Baer, 1959) and possibly to 8-MOP. But, as many workers in this field have pointed out, this is not so: the action spectrum of 8-MOP differs markedly

\* As far as we know, furocoumarins have not been chemically identified in oil of persian lime, but our results suggest that they may be present.

from its absorption spectrum. The latter is well known (Lerner *et al.*, 1953) and is shown in Fig. 4 (left-hand curve), which was obtained with a photoelectric spectrophotometer (Hilger "Uvispek") from 8-MOP dissolved in chloroform. Absorption is greatest at and below 250  $m\mu$  with a lesser peak around 300  $m\mu$ ; in our experiments, however, no significant potentiation of erythral responses was found in these regions. The reason for this is not clear.

It will be seen that the wavelengths at which the smallest amount of energy is needed to produce an effect with 8-MOP is usually 320  $m\mu$ . This point how-

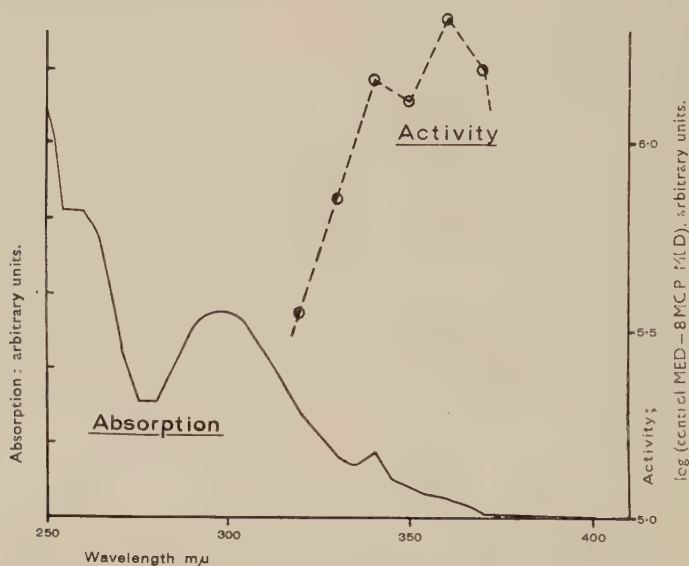


FIG. 4.—Comparison of absorption and action spectra of 8-MOP. Vertical scales are in different units and the curves should be compared only on the wavelength scale.

ever cannot be regarded as the peak of the action spectrum. If from 320 to 370  $m\mu$  the average of the MED values for skin treated with 8-MOP is subtracted from that for normal skin, maximal reactivity is seen to lie between 340 and 370  $m\mu$ . On average, the most effective wavelength is 360  $m\mu$  (see Fig. 4, right-hand curve). That this is the actual peak of the action spectrum must however be regarded with caution, as the errors inherent in our experimental procedure are probably large.

When the action spectrum of oral 8-MOP is considered, we are clearly not in a position to come to any conclusions as our data are incomplete. Clearly, however, this psoralen is much more active when used locally. But so far there is no reason to suppose that the range of spectral reactivity produced by 8-MOP differs when it is used orally and topically.

Sunburn sustained through light cotton shirting is unusual in an English



summer. This is due to the fact that radiant energy of the normal sunburn spectrum (280–320  $m\mu$ ) cannot penetrate cotton clothing effectively because it is scattered. But radiation of longer wavelengths may possibly be scattered less than that of the sunburn spectrum and so enough may reach skin sensitized with 8-MOP to produce erythema. It is also important that the relative intensity of sunlight in the range 320–370  $m\mu$  is considerably greater than that at 280–320  $m\mu$ .

#### SUMMARY.

Preliminary studies of the action spectrum for the erythema response of human skin to 8-methoxypsoralen suggest that its spectral reactivity lies between 320 and 370  $m\mu$ . Least energy for an effect in skin treated with 8-MOP is generally required at 320  $m\mu$ . The maximum of the action spectrum, however, may lie at 360  $m\mu$ .

The action spectrum of 8-MOP differs considerably from its absorption spectrum.

It is possible to obtain erythema and tanning from sunlight on skin painted with 8-MOP, even though the painted area is clothed.

Dr. T. B. Fitzpatrick very kindly supplied us with the oral preparation of 8-MOP. The Medical Research Council of Great Britain generously defrayed expenses arising from the purchase of apparatus.

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#### ADDENDUM.

Since this paper was submitted, Pathak and Fellman (1960) *Nature, Lond.*, **185**, 382, have published observations on the fluorescence spectra of the psoralens and have suggested that, where biologically active, these compounds should sensitize skin at 340–380  $m\mu$  and 8-MOP, in particular, at 360  $m\mu$ .

# HYPERAEMIA OF THE DEEPER CUTANEOUS VESSELS AFTER IRRADIATION OF HUMAN SKIN WITH LARGE DOSES OF ULTRA-VIOLET AND VISIBLE LIGHT.

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"IMMEDIATE pigmentation" is described as a brownish-red or greyish discoloration of human skin provoked by heavy doses of long-wave ultra-violet and visible light (320–450  $m\mu$ , Hamperl *et al.*, 1939; Wiskemann and Wisser, 1956; Wisser, 1955). It develops during the irradiation, in contrast with the normal sunburn pigmentation, which accompanies the erythema some days after an irradiation with small doses of short-wave ultra-violet light (297  $m\mu$ ). This immediate pigmentation partly fades within one or two hours after the irradiation but leaves some traces for a rather long time. Its cause is supposed to be the darkening of premelanin which is already present.

Our attempts to reproduce this phenomenon have lead to the observation of a different effect which will be explained in this communication.

## THE APPARATUS.

The light source is a water cooled super high-pressure mercury lamp (SP 500, Philips) with a glass cover. A natural size image ( $15 \times 2$  mm.) of the arc is thrown on to the skin by means of two glass lenses each of 4 cm. diameter and 10 cm. focal length. To isolate the single wave lengths 366, 405 and 436  $m\mu$  as they are emitted by the mercury arc, interference filters (Balzers) are used with measured transmissions of 23, 38 and 40% respectively and with a half peak width of 22, 14 and 10  $m\mu$ . The light obtained in this way is sufficiently monochromatic to exclude the wave-lengths near 300  $m\mu$ , for which the skin has such a great sensitivity. Contamination with radiation of these wavelengths might obscure the interpretation of the results of irradiation with the longer wavelengths.

The intensity of the image of the arc of the SP 500 at 297  $m\mu$  without filtration would be about 200 mW/cm.<sup>2</sup> Before reaching the skin however, the radiation has to pass through three layers of glass, each having a transmission of less than  $10^{-2}$ .

The interference filters, which are mounted between the glass lenses, have at 297  $m\mu$  a transmission of less than  $10^{-3}$ . Therefore, the intensity of 297  $m\mu$  on the skin is less than  $200 \times 10^{-9}$  mW/cm.<sup>2</sup> With an irradiation time of 15 minutes, less than  $2 \times 10^{-4}$  mWsec./cm.<sup>2</sup> of 297  $m\mu$  falls on the skin. Our measurements have indicated that the mean dose of 297  $m\mu$  (MED 297) to provoke a minimum erythema on the upper arm is 25 mWsec./cm.<sup>2</sup> Thus, with an irradiation time of 15 minutes at the wave-lengths 365, 405 or 436  $m\mu$ , the upper arm does not receive more 297  $m\mu$  than one-thousandth of the MED 297.

The intensity at the centre of the image on the skin at 366, 405 and 436  $m\mu$  has been found to be 290, 380 and 450 mW/cm.<sup>2</sup> (the calibration data of the manufacturers of the thermopile, Kipp, Delft, were used). Therefore, with an irradiation time of



1 minute on the upper arm the doses correspond respectively to 700, 910 and 1080 times the mean MED 297.

Fig. 1 shows the apparatus fixed to a quartz spectrograph which is used to irradiate the skin with 297 and 257  $m\mu$  (Rottier, 1953). The housing of the lenses and filters of the apparatus is water cooled, the filter itself is cooled by a stream of nitrogen.

The whole equipment is mounted in a device by which any desired position can be obtained for the irradiation of the skin on any part of the body.

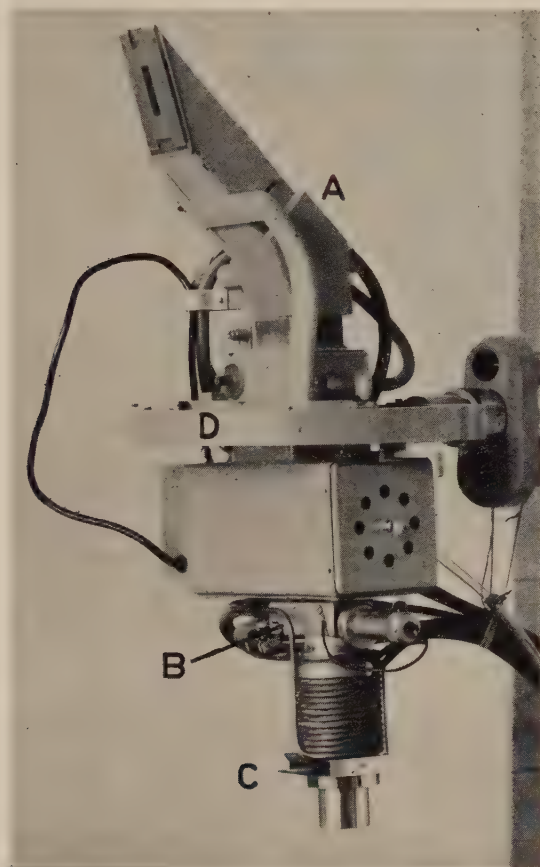


FIG. 1.—Apparatus for irradiation of skin with monochromatic light of wave-lengths 257, 297, 366, 405 and 436  $m\mu$ . A. Quartz spectrograph for 257 and 297  $m\mu$ . B. SP 500 super high-pressure mercury arc. C. Housing of lenses and interference filter. D. Supporting ring.

### RESULTS.

The skin of the upper arm of 16 patients was tested for its reaction after irradiation with 257, 297, 366, 405 and 436  $m\mu$ . With the wave-lengths 366, 405 and 436  $m\mu$ , irradiation times up to 15 minutes were used, resulting in visible reactions in all cases except one which proved to be very insensitive. The reactions in the other 15 cases were complexly different. In this communication only the immediate reactions will be discussed.

With 366  $m\mu$  and irradiation times varying from 1 to 10 minutes, in 7 out of 15 cases an immediate erythema was observed lasting for not longer than 3 to 5 minutes. Since such irradiations raise the skin temperature by  $1.5-3.5^{\circ}$  C., we are inclined to ascribe such erythemata to this increase in temperature. Two of these cases also showed oedema lasting about half an hour. In another of these 7 cases, the red colour of the immediate erythema changed within some minutes to a greyish-violet, lasting about half an hour. Here we come to the discoloration which is of special interest.

This greyish-blue to brownish discoloration, which was visible immediately after the irradiation, was observed in 7 of the 15 cases studied. It gradually faded and lasted for not more than 2 hours. As mentioned above, in one case the bluish discoloration of the skin was preceded by erythema for some minutes, while in another case it was accompanied by oedema. It is difficult to indicate the moment when the bluish-grey discoloration disappeared. Sometimes a very slight violet or pink or brownish hue persisted for 1 or even 2 days. The minimum irradiation time to provoke the effect with 366  $m\mu$  varied from 1 to 8 minutes (administered doses 17-140 Wsec./cm.<sup>2</sup>). In cases where it was elicited by 366  $m\mu$ , it was also seen after irradiation with 405 and 436  $m\mu$ . The last two wavelengths necessitated longer irradiation times (3 to 12 minutes) than 366  $m\mu$  (administered doses 70-320 Wsec./cm.<sup>2</sup>).

#### EXAMINATION OF THE GREYISH-BLUE DISCOLORATION.

Seeing this discoloration for the first time we thought it was "immediate pigmentation", but when pressure was exerted with a piece of glass, it was always possible to make the colour disappear, certainly during the first half hour of its existence. Later, when it was still visible, the effects of pressure were sometimes indecisive. It was then possible to see a faint yellowish-brown trace of colour. The perceptibility of these discolorations naturally depended greatly on the initial colour of the skin. When the skin was well pigmented, the bluish-grey colour was evident for not longer than one hour, disappeared completely under pressure and did not persist. When the skin was fair or whitish, some persistence could be seen for 24 hours or even longer and the hues were more difficult to describe. It was particularly difficult to judge whether these persistent colours remained visible under pressure.

In a case of xeroderma pigmentosum in a woman of 18 years, showing the blue-grey discoloration on her rather greasy skin, some experiments were performed to see if the effect consisted of an oxidation of some fatty substance in the sebum. Cleansing with alcohol, ether and even oxidation with potassium permanganate followed by bleaching the heavily stained skin with sodium hyposulfite, had no influence on the effect. Stripping of the uppermost layers of the stratum corneum by applying adhesive tape four times in succession



had no effect. Pricking a drop of 0.1% adrenaline into the skin at a site which was discoloured by irradiating for 8 minutes with 366 m $\mu$ , immediately caused a distinct blue spot with a diameter of 3 mm. to become visible. Some ten minutes later, this blue spot was surrounded by a whitish ring. Half an hour later the effects had almost disappeared.

#### DISCUSSION.

The experiment of pricking adrenaline through the epidermis in a bluish spot caused by irradiation with a heavy dose of long-wave ultra-violet light was suggested by the impression that the discoloration might originate in hyperaemia of the deeper vessels of the skin.

Indeed, we saw an analogy between this discoloration by light and the normal blue colour of the subcutaneous veins.

Adrenaline contracts the arterioles with the result that whitish patches develop. In our experiment, however, a blue patch developed which was surrounded 10 minutes later by a whitish ring at some distance (about 2 mm.) from the spot where the adrenaline entered the skin. We do not understand the mechanism of the development of the blue patch. But from the failure to develop a white patch we can conclude that the arterioles were paralysed by ultra-violet irradiation and irresponsive to adrenaline. We therefore regard the bluish-grey discoloration discussed here as blue hyperaemia of the deeper vessels of the skin.

It is generally accepted that the short-wave ultra-violet erythemata caused by 250 and 297 m $\mu$  are due to capillary dilatation and that these wavelengths penetrate only very superficially into the skin. On the other hand, the longer wavelengths penetrate much deeper and certainly well below the epidermis (Rottier, 1954). Therefore it is quite feasible that these wavelengths cause dilatation of the vessels of the subpapillary plexus. A great difference, however, from the capillary erythemata, which take some hours to develop after irradiation, is the immediate appearance of the blue hyperaemia. Whereas for an explanation of the capillary erythemata the action of chemical mediators is judged to be necessary, in the case of the blue hyperaemia a direct action of the light on the vessels may be surmised. As to the faintly visible residua, it is tempting to ascribe these to cellular infiltrations around the reacting vessels.

Two points remain to be mentioned. First, the blue hyperaemia is elicited only in about half of the cases studied. Other visible responses to these irradiations, all vascular, are equally frequent. So different reaction patterns of the blood vessels must exist in different skins.

Second, in cases of light dermatoses it is important to realize that long-wave ultra-violet light, which is transmitted by glass, and which is always present

in daylight, and even in violet and blue visible light, may influence the vascular behaviour of the skin unfavourably by causing vasodilatation.

#### SUMMARY.

By giving large exposures of long-wave ultra-violet ( $366\text{ m}\mu$ ) and visible light ( $405$  and  $436\text{ m}\mu$ ) a bluish-grey discoloration can be elicited in the skin. This discoloration disappears when pressure is exerted with a piece of glass and therefore is explained as a hyperaemia of the vessels of the subpapillary plexus. It was seen in about half of the cases examined. The other cases exhibited mostly erythema. The so-called "immediate pigmentation" has not been observed, not even with a dose 10,000 times as strong as that necessary to provoke the normal sunburn erythema.

We gratefully acknowledge the help of Miss P. Dales who performed the irradiations.

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## POLYMORPHIC LIGHT ERUPTION.

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THERE have been previous experiments designed to determine the wavelengths responsible for polymorphic light eruption. The techniques and light sources employed, however, are inadequately described and the responsible wavelengths are not precisely stated.

### REVIEW OF THE LITERATURE.

Veiel (1887), by a simple experiment using a red veil as a filter and the sun as the source of light, proved that his patient's eczema solare was uninfluenced by the heat rays of the sun, but that the other rays perpetuated it. The first controlled experiments were performed by Haxthausen in 1919. In his thesis, he reported clinical and experimental observations on thirty patients with polymorphic light eruptions. Unfortunately his thesis was not available to me and his later work (Hausmann and Haxthausen, 1929) based on these data, refers to them only briefly. In two cases of "juvenile type" tested by Barber *et al.* (1926), one showed no immediate response and the other only slight erythema. In the first, papules and vesicles appeared on the second day without preceding erythema. The results obtained by Sellei and Liebner (1926) are unique. They described eight patients, in whom urticaria-like papules and excoriated and lichenified skin lesions were the prominent features. In some patients the eruption extended to the covered parts. The irradiation of uninvolved skin exacerbated the existing lesions; irradiation of the involved skin aggravated the irradiated lesions and caused new crops of pruriginous papules to appear on the healthy skin. The authors were able to elicit this reaction with both actinic and infra-red rays. The patient of Urbach and Konrad (1929) was sensitive to the yellow-red part of the visible spectrum. The test reproduced the original lesion. Amato (1926) reported a patient aged 31 who, annually from the onset of menstruation at 16, developed a recurrent eruption on exposure to sunlight. This was particularly pronounced during menstruation. A temporary x-ray menopause resulted in temporary improvement, but the condition relapsed with the reappearance of menstruation. Mühlman and Akobjan's patient (1930), aged 17, reacted to sunlight under experimental conditions with a papulo-vesicular eruption which took seven days to clear. A woman aged 45 shown by Lomholt (1930) had suffered from a severe dermatitis since childhood. Detailed study with a filtered carbon arc light showed increased sensitivity to rays of 2800 to 3500 Å, whereas 3800 Å and longer had no harmful

effect. An increased sensitivity limited to the emission of a quartz lamp was observed by Carrié (1931). The hypersensitivity was of short duration. The patient of Gläubersohn and Goldenberg (1930) reacted with urticarial wheals to ultra-violet irradiation. The clinical picture consisted of urticaria and eczema solare with papulo-vesicles. Liebner's (1931) patient was sensitive to the unfiltered and yellow rays of the quartz lamp which produced the rash. A patient reported by Templeton and Lunsford (1932) reacted to sunlight with mild erythema. The clinical manifestation was a diffuse, dry, slightly squamous dermatitis. Bernstein's (1933) patient with eczema solare reacted only to mercury quartz irradiation. He responded with an abnormal erythema which eventually changed into an eczematous reaction. When the Solux lamp was used, no reaction ensued. Gilfillan (1937) produced only an erythema in a cowman who developed acute light sensitivity when he was treating a cow with lysol compounds and a white ointment.

Blum, whose work is the most comprehensive in this field, had the opportunity of investigating four such cases. In 1935 he studied a patient with eczema solare. Corning filter 774 which transmits wave-lengths longer than about 3000 Å protected the patient against a mercury arc, but did not completely prevent the development of lesions when the patient was exposed to direct sunlight for forty minutes. On the first occasion there was an erythematous response which became eczematous: on the second there was persistent erythema. Two light tests carried out at an interval of eight months in his second patient showed the following features; when first tested, the patient responded with a mild erythema after moderate exposure to sunlight; this test was regarded as negative. When re-tested, erythema developed after a short exposure and was followed by a scaly eczematous eruption, somewhat resembling the original lesion. No lesion developed when the irradiation was filtered through window glass or other filters which removed wavelengths shorter than 3150 Å. In Blum's (1937) third patient, a woman aged 40, with an erythema of the exposed parts, mercury radiation shorter than 3200 Å elicited erythema. An erythematous dermatitis developed at the test sites; a fourth case (1940) reacted with a normal erythema to the mercury arc, whereas carbon arc radiation elicited the lesions.

Wavelengths longer than 3200 Å failed to produce any visible changes in a patient investigated by Schaumann (1932) and Schaumann and Lindholm (1938). Filters were used, with the sun as the source of irradiation. Turner's (1939) patient was sensitive to the wavelengths 2900 Å to 3200 Å. The patient, a man aged 44, responded with an abnormal erythema. The clinical picture was of a red eruption of the face, neck and backs of the hands associated with an itching and burning sensation. Depending on the duration of the exposure, Burekhardt's patient (1942) reacted either with simple erythema, or with papules and vesicles. Clinically the patient had a polymorphic light eruption.



In four of five cases of prurigo aestivalis investigated by Epstein (1942), the response to ultra-violet light was abnormal with prurigo-like nodules appearing after various intervals. In one case, a normal reaction to ultra-violet light was noted. In the only case of prurigo aestivalis with eczema solare that was studied, the reaction of the unaffected skin was less than in normal people. Both cases of eczema solare responded only with erythema to sunburn irradiation. Both patients in whom prurigo aestivalis, eczema solare and urticaria solare were the clinical features responded with an immediate urticarial reaction: in one of them, prurigo-like lesions developed later. The only case of prurigo aestivalis and urticaria solare investigated gave the normal response to ultra-violet light. These tests were performed mainly with the Kromayer lamp, but in a few patients Hanovia and carbon arc were also used. According to the author, the filters used permitted a clear determination of the active wavelengths in some of the cases only.

Zenmer and Bentnagel (1950) reported two patients, a man aged 53, and a woman aged 57, suffering from a dermatitis of the exposed skin who were abnormally sensitive to ultra-violet and visible light in the one instance, and to ultra-violet light alone in the other. A patient with eczema solare examined by Russell and Anderson (1950) produced a fourth degree erythemato-bullous reaction to an exposure which usually produced a first degree erythema in normal people. Two patients reported by Kesten and Slatkin (1953) were sensitive to wavelengths shorter than 3400 Å. The type of reaction was not stated. Wiskemann and Zimmermann (1956) reported four patients belonging to two families showing erythema and oedema of short duration to wavelengths of 3120 Å to 6150 Å. Scott and Molhuysen van der Walle (1958) found in their patients with "dermatitis solaris" an increased sensitivity to the short sunburn spectrum while in cases of "prurigo aestivalis" it was diminished.

#### INVESTIGATIONS.

##### *Apparatus and Method.*

The monochromator used for this investigation consisted of a high-intensity quartz mercury lamp fitted with an air and water cooling system and a transformer and a quartz spectroscope composed of a collimator and a prism. The spectral range of the lamp was from 2200 Å to 11,000 Å, with the highest intensity in the ultra-violet spectrum and a break due to the absorption of the mercury vapour at 2536 Å. The steadiness of the intensity of irradiation was controlled with a selenium photoelectric cell with the highest sensitivity in the green part of the spectrum. A uranium plate served to check its completeness. The whole spectrum was projected on to the region between the scapulae for 1, 5 and 15 minutes, and the responses were read after 6 and 24 hours with the aid of a photographic plate bearing the wavelength scale of the monochromator. Because of the small erythema producing potency of the lamp in range of ultra-violet A, the patients were also tested with a Kromayer lamp using filters.

To appreciate the principles underlying these tests and their interpretation, some understanding of "E-viton value" is necessary. The term is employed to indicate

the relative erythematous output of a source in different wavelengths of the ultra-violet spectrum. For the lamp used it was as follows: ultra-violet C consisted of 993,600, ultra-violet B of 2,552,000 and ultra-violet A of only 26,200 E-vitons. If in a light-sensitive person erythema was produced by ultra-violet B after an exposure of 5 minutes, and assuming that the degree of sensitivity to ultra-violet B was equal to that to ultra-violet A, then an exposure of approximately 485 minutes would produce an erythematous response in the band of ultra-violet A.

The filters and their transmissions were deep violet (3800–4500 Å), blue (4400–4900 Å), blue-green (4700–5200 Å), yellow-green (4700–5200 Å), orange (5750 Å onwards) and a microscope slide (3200 Å onwards).

The skin was also directly exposed to the Kromayer lamp from a distance of 1 cm. through a lattice cut in black paper and composed of seven holes each 1 cm. square. The skin was exposed for 1 second longer through each successive square, the shortest exposure being 1 second and the longest 7 seconds. An exposure to only a few wavelengths would yield more precise results. Such a procedure would entail exposures of many hours' duration to which few patients would agree. Moreover, the different parts of the back on which these numerous tests would have to be performed are not equally light sensitive and this would reduce the value of the technique. All exposure times were arbitrarily chosen but were based on the average response of forty controls of various ages and complexions. Nineteen patients with polymorphic light eruption were studied. The pertinent data are summarized in Table I.

## RESULTS.

The division of the ultra-violet spectrum into ultra-violet A, B and C is arbitrary but seems to be of some practical convenience.

### *Response to Ultra-violet A.*

(i) Immediate response. Immediate pigmentation with or without late erythema was observed in only 5 cases (26%), less frequently than in normal controls. Immediate erythema of short duration occurred in 14 patients (74%), compared to 27% in controls.

(ii) Late erythematous response. In all patients an abnormal sensitivity was noted. Periods of exposure which in controls did not produce any reaction of only direct pigmentation, produced erythema in light-sensitive patients, not differing from that produced by total ultraviolet irradiation. The minimal erythema exposure, i.e. the duration of exposure needed for the development of barely perceptible erythema, though beyond the limits of normal, was not the same in all patients. The filter transmitting wavelengths of 3200 Å and longer also transmitted a few wavelengths shorter than 3200 Å, the role of which in the producing erythema, though negligible, cannot be completely ignored.

### *Responses to Ultra-violet B.*

The erythema produced by ultra-violet B is indistinguishable by clinical inspection from that produced by ultra-violet A or C. Since the response to



TABLE 1.—*Clinical Data on Nineteen Patients with Polymorphic Light Eruptions.*

## POLYMORPHIC LIGHT ERUPTION

265

| Sex. | Age. | Age of onset. | Dura-<br>tion. | Month of onset. | Pattern of the reaction. | Distribution.                                           | Occupation.          | Eye colour. | Hair colour. | Skin pigmentation. | Hyper-sensitivity to ultra-violet |   |   |   | Im-<br>mediate pigment-<br>ation. | Dermo-<br>graph-<br>ism. | Response to treatment. |
|------|------|---------------|----------------|-----------------|--------------------------|---------------------------------------------------------|----------------------|-------------|--------------|--------------------|-----------------------------------|---|---|---|-----------------------------------|--------------------------|------------------------|
|      |      |               |                |                 |                          |                                                         |                      |             |              |                    | A                                 | B | C |   |                                   |                          |                        |
| F    | 20   | 16            | 4              | March           | Papular                  | "V" of the neck, fore-arms and legs                     | Copy-typist          | Blue        | Fair         | Light              | +                                 | + | + | — | Normal                            | Completely controlled.   | Ditto.                 |
| M    | 80   | 60            | 20             | June            | Plaque                   | Face, neck and back of hands                            | Retired policeman    | Grey-blue   | Brown        | Moderate           | +                                 | + | + | + | Wheal                             | Completely controlled.   | Ditto.                 |
| "    | 37   | 36            | 1              | Feb.—March      | Papular                  | Face                                                    | Railwayman           | Brown       | "            | "                  | +                                 | + | + | — | Normal                            | "                        | "                      |
| "    | 25   | 24            | 1              | April           | "                        | Face, neck, "V" of the neck and back of hands, forearms | Agri-cultural worker | "           | "            | "                  | +                                 | + | + | + | "                                 | No effect.               | "                      |
| F    | 56   | 16            | 40             | March           | "                        | Face and back of hands                                  | Housewife            | Grey        | Fair         | Light              | +                                 | + | + | — | Wheal                             | Not seen again.          | Alleviated.            |
| "    | 43   | 35            | 8              | April           | "                        | Ditto                                                   | Waitress             | Blue        | "            | "                  | +                                 | + | + | — | Normal                            | Wheal                    | Completely controlled. |
| "    | 21   | 9             | 12             | March           | "                        | "                                                       | "                    | Grey        | "            | "                  | +                                 | + | + | — | Normal                            | Not seen again.          | Ditto.                 |
| M    | 42   | 27            | 15             | "               | "                        | Face, neck and back of hands                            | Driver               | Green       | "            | "                  | +                                 | + | + | — | "                                 | "                        | "                      |
| F    | 49   | 49            | —              | June            | Plaque                   | Face, neck, back of hands, forearms and arms            | Housewife            | Green       | "            | "                  | +                                 | + | + | — | "                                 | "                        | "                      |
| "    | 17   | 7             | 10             | April           | Papular                  | Face, back of hands and legs                            | Schoolgirl           | Blue        | Fair         | "                  | +                                 | + | + | — | "                                 | Completely controlled.   | Alleviated.            |
| M    | 51   | 48            | 3              | March           | "                        | Neck, back of hands and forearms                        | Grocer               | Hazel       | Brown        | "                  | +                                 | + | + | — | "                                 | "                        | "                      |
| "    | 62   | 56            | 6              | June            | Eczematous               | Face and back of hands                                  | Dental surgeon       | Blue        | "            | "                  | +                                 | + | + | — | Normal                            | Slightly improved        | Alleviated.            |
| F    | 52   | 32            | 20             | March           | Papular                  | Neck                                                    | Housewife            | "           | Fair         | "                  | +                                 | + | + | — | "                                 | Wheal                    | Not seen again.        |
| M    | 72   | 67            | 5              | "               | Plaque                   | Ditto                                                   | Bricklayer (retired) | "           | Brown        | "                  | +                                 | + | + | — | Normal                            | Ditto.                   | "                      |
| "    | 53   | 52            | 1              | June            | Papular and eczematous   | Face and forearms                                       | Roadman              | "           | Fair         | "                  | +                                 | + | + | + | "                                 | Not seen again.          | Ditto.                 |
| "    | 46   | 46            | —              | Feb.            | Eczematous               | Face and back of hands                                  | Farmer               | Brown       | Brown        | Moderate           | +                                 | + | + | — | "                                 | Alleviated.              | "                      |
| F    | 41   | 33            | 8              | March           | Papular                  | Ditto                                                   | Housewife            | "           | "            | "                  | +                                 | + | + | + | "                                 | Not seen again.          | Completely controlled. |
| "    | 26   | 7             | 19             | "               | "                        | "                                                       | "                    | Grey-blue   | Fair         | Light              | +                                 | + | + | — | "                                 | Not seen again.          | "                      |
| "    | 61   | 51            | 10             | "               | "                        | "                                                       | "                    | Brown       | Brown        | Moderate           | +                                 | + | + | + | "                                 | Not seen again.          | "                      |

these wavelengths is readily elicited both in normal and light sensitive patients, the true hypersensitivity was only determined by the evaluation of the response to both the monochromator and Kromayer lamp without filters. All patients showed an increased sensitivity to ultra-violet B.

#### *Response to Ultra-violet C.*

Hypersensitivity to this part of the spectrum was easily observed and read when the monochromator was used. The width of the band of erythema was not the same in all patients, which clearly showed that the same wavelengths were not involved in the reaction in every case. The erythematous response did not differ from that to ultra-violet B, with which it fused.

#### *Other Filters.*

With no other filter could a reaction of the skin be obtained.

### DISCUSSION.

The light sensitivity found in all the patients was elicited by the whole ultra-violet spectrum.

It may be significant that such a small number produced immediate pigmentation after irradiation with ultra-violet A in contradistinction to erythema produced by the same wave-lengths. Normally, approximately 13% of the population react with erythema alone to a sufficiently long exposure to ultra-violet A rays: 67% react with immediate pigmentation and erythema and 20% with immediate pigmentation only (Schulze, 1956). The percentage found in this series of light sensitive patients is almost the opposite. The absence of immediate pigmentation, which depends on the oxidation of preformed pigment present in the epidermis in its colourless form (Henschke and Schulze, 1939; Schulze, 1949), suggests that the early protection against sunlight which immediate pigmentation offers is lacking in these patients. This, however, does not mean that its absence is a prerequisite for the development of a polymorphic light eruption; this is also often found in normals with fair complexion, and in the majority of light sensitive patients. It can therefore only be said that the absence of immediate pigmentation may predispose such people to light sensitivity.

The failure to pigment found in nearly all the patients, manifesting itself as an immediate erythema (instead of pigmentation) with ultra-violet A and easy sunburning due to ultra-violet B, certainly suggests some role of the pigment in the protection of the skin greater than the present tendency shows. Immediate pigmentation has no direct bearing on pigmentation produced by ultra-violet B (Henschke and Schulze, 1939); a closer relationship between

them, however, must be postulated when their protective rôles are considered. It is illogical to deny to melanin formed from leucomelanin in the Malpighian layer the same properties which it exhibits when situated in the basal layer.

All light-complexioned people (in the wider sense) may be regarded as having a more or less "diffuse anomaly of pigment protective capacity". This physiological trait lessens their ability to screen the deeper layers of the epidermis and the dermis as effectively as darkly pigmented people; the liability to develop abnormal patterns of reaction is increased. The poor pigmentary capacity of these individuals is a contributory factor but not of course the cause of the hypersensitivity to light itself.

The other physiological protection against sunlight—thickening of the horny layer—seems to be unimpaired in patients with polymorphic light eruption. The horny layer is, however, thinner in light-complexioned people than in dark; this may also contribute to their greater susceptibility to sunburn.

By analogy with the findings with ultra-violet C, it is reasonable to assume that the degree of reaction also depends on the numbers of wavelengths to which the individual reacts. The sensitivity, however, never extended beyond 3800 Å. More intense reaction could be conceived as the summation of the reactions to contiguous wavelengths. It is also possible that, as observed in two patients with urticaria solare, in addition to variation in the number of wave-lengths involved, there is also a difference in the degree of hypersensitivity to individual wavelengths.

Late erythematous response was also noticed to exposures which in controls give only an immediate pigmentation or no response at all. The same wave-lengths, however, if applied for a sufficiently long time, would also produce late erythema in controls.

In this series, the clinical picture was reproduced experimentally in one case only; in the remainder the response was limited to erythema. Provocation of prurigo lesions was reported by Haxthausen (1919), Urbach and Konrad (1929), Goeckermann *et al.* (1929), Mühlmann and Akobjan (1930), Schaumann and Lindholm (1938), Burckhardt (1942) and Epstein (1942); eczema solare by Veiel (1887) and Blum *et al.* (1935). Either erythema or changes identical to the existing ones were produced depending on the source of irradiation used (tungsten electrodes, carbon arc, mercury quartz or Solux) by Barber *et al.* (1926) and Bernstein (1933). Either a normal erythema or changes identical to the existing ones, depending on the site irradiated, were reported by Sellei and Liebner (1926). Other investigators, e.g. Rost and Keller (1929), obtained only an erythema, which three to four days later was replaced by a picture similar to the clinical state. Möller (1900), Martenstein (1922), Funfack (1924) and Schreus (1934) showed that only after repeated exposures can typical papules be produced, the first response being normal or less than normal erythema. Sellei (1930) stated that in polymorphic light eruption there is



hypersensitivity to quartz lamp, but that this alone cannot reproduce the complete clinical picture.

Summing up the experimental responses of the skin, it is seen that they are inconstant, often inconsistent and sometimes contradictory. Insufficient intensity of light in the active region of the spectrum, inadequate exposure and fluctuations in the patient's threshold of sensitivity are given as explanations. Though I agree with these possibilities, I think that more important for the explanation of the experimental response is the mode of action of light under natural and experimental conditions. Under natural conditions, exposure is intermittent and prolonged over many days, thus allowing the interference and interaction of additional factors, whilst under experimental conditions the period of exposure is brief and reproduces only one of the normal factors and that only partially. An analogy with the patch test can be drawn, the latter not always reproducing the clinical picture of the condition.

The natural clinical picture is often further modified by scratching and sometimes by self-medication. The importance of scratching must not be overestimated, but in some patients whose response to repeated physical trauma of this type is abnormal, in that they lichenify, the effect may be considerable. Thus the clinical picture, although originally produced by light, may be further influenced by other contributory factors, exogenous or inborn.

#### CLINICAL STUDY.

The clinical features and response to ultra-violet light are summarized in Table I.

I most frequently encountered the summer prurigo type of polymorphic light eruption; this is in contrast to Lamb's (1957) series in which the plaque type predominated. There were no cases in my series of the erythema multiforme type; I believe that erythema multiforme confined to the exposed parts and apparently provoked by sunlight are not produced by the same mechanism as other types of polymorphic light eruption. It appears to be identical to erythema multiforme of non-exposed skin with sunlight as a non-specific localizing factor.

The sexes were equally affected. Sarateanu (1938) found 64 cases in the literature up to 1938, of which 58 were in females. In a recent study Cahn *et al.* (1953) found 9 females and 8 males. Patients of any age can be affected. It is however more frequent among older people.

The duration of the light sensitivity ranged between one month and 40 years. It seems that the condition does not become less severe with the passage of time. However, a decrease in the degree of the reaction during the course of the year has repeatedly been noted. This can be likened to the "hardening effect" in industrial dermatitis. The reaction recurs the following year with

the same intensity, the absence of sunlight during the winter enabling the organism to regain the capacity to react. The gradual decrease of light sensitivity during the summer may be the result not only of the thickening of the horny layer, but also of true hyposensitization. The onset of the skin reaction usually occurred during the first month of spring. Besides the increased intensity in ultra-violet A and B, the hours of sunshine then also become more numerous. Satisfactory results were obtained with chloroquine.

Only one instance of familial light sensitivity was noticed. The patient, as well as her brother and sister (who were not examined) suffered from what was probably a light sensitivity eruption. In the pertinent literature, familial light sensitivity was recorded by Sellei and Liebner (1926) and Burckhardt (1942), both in 2 sisters, and by Nobl (1915), Glaubersohn and Goldenberg (1930), Russell and Anderson (1950) in one parent and one or more children. There was no consanguinity of the parents. This fact, together with the rather unsatisfactorily small pedigrees which can be compiled from the articles mentioned, suggest that when a predisposition to polymorphic light eruption is inherited, it is transmitted as a dominant character.

The majority of my male patients (seven out of nine) were obliged by their occupation to remain out of doors the greater part of the day. The preponderance of outdoor workers among such patients was also noticed by Cahn *et al.* (1953) and Epstein (1942).

Mention has been already made of the complexion of my patients. The study of eye and hair colour and complexion of light sensitive individuals has rarely been recorded. The absolute figures have no significance unless they are compared with the figures for random control subjects from the same population group. This I have attempted. It follows from the comparison of these two groups that the colour of the eyes and the complexion of the patient are the two most reliable criteria for the clinical assessment for the predisposition for light sensitivity. Blue eyes are found nearly twice as often in light sensitive people, and brown twice as rarely. Lightly pigmented people are also found twice as often among the light sensitive group. Although moderately pigmented people represented 30%, which suggests strongly that poor pigmentary capacity is not the only factor in light sensitivity, it is of interest that no instance of the latter occurred among heavily pigmented people. Hair colour seems to be the least reliable factor. Blonde and shades of brown are found in almost the same percentage in normal and light sensitive individuals. Two extremes, red and black, did not occur in my series.

An attempt was also made to correlate the reaction of blood vessels to light with that provoked by mechanical stimulation. My figures suggest that the incidence of dermographism is no higher in patients with polymorphic light eruption than in normal controls. Similar conclusions have been reached for other types of physical allergy.

## SUMMARY.

The results of earlier reported experimental investigations of polymorphic light eruption are reviewed. The author's own method and findings are given. Increased light sensitivity in the ultra-violet band of the spectrum was found in the patients investigated. The clinical features of the cases are compared with those found in the literature.

These investigations were carried out in the Department of Dermatology, Addenbrooke's Hospital, Cambridge, under the supervision of Dr. A. J. Rook, during the tenure of the Trinity College bursary (1955-57) to Cambridge University.

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## SUN SCREENING SUBSTANCES.

### THEIR PHYSICAL EVALUATION AND CLINICAL APPLICATION.

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IN THE PRESENCE of abnormal sensitivity to light or anticipated excessive exposure, the physiological mechanism of protection requires supplementation by artificial measures. As physical methods of protection are often impracticable or cosmetically unacceptable, a chemical sunscreen is normally employed.

As far as I can discover, Veiel (1887) was the first to use such a protective cream in the treatment of a photodermatosis. He treated his patient, a woman with "eczema solare", with tannic-salicylic acid combined with sulphur. Tannic acid is still used for the same purpose. Another sunscreen which was used in the early days and which has stood the test of time is aesculin. In the form of its monoxo and dimethylamino derivates it was introduced by Unna (1911) instead of "curcuma", which was coloured and for that reason unsatisfactory for external application.

#### PREVIOUS INVESTIGATIONS.

The protective capacity of some substances was first experimentally investigated by Freund (1911). He performed spectrophotometric measurements on lanolin, vaseline, simple lard, aesculin and Unna's ointment. Morse (1936) investigated the opacity of emulsions in the visible part of the spectrum. He was more concerned, however, with the reflection of emulsions than with absorption. Though often quoted, his work has no direct bearing on the therapeutic use of sunscreens. The method used by Strandberg (1933) did not allow him to determine quantitative absorption at different wavelengths. Luckiesh *et al.* (1946) undertook investigations for military purposes and obtained very satisfactory protection with dark red veterinary petrolatum and 10% salol. Lorentzen (1955) tested 0.05 mm. layers of various bases between two quartz plates, using a Beckmann spectrophotometer. He investigated adeps lanae, vaselinum flavum and album, axungia, ung. cerac, eucerin, silicone, carbowax and benzocaine. Russell (1950) carried out investigations along the same lines, together with tests on the back of a patient with eczema solare. He investigated a vanishing cream, the composition of which was given, tannic acid, quinine hydrochloride, pyribenzamine, sodium para-aminobenzoate and salol. The degree of absorption at various wavelengths can not be seen from these experiments. Giese (1946) used a mercury vapour

lamp as source of irradiation, investigating the protective power of several substances on human skin. The same source was also used by Tronnier and Klusmann (1956) and similar artificial sun sources were used by Henschke (1940), Kimmig (1955) and Wiskemann and Zimmermann (1956).

The use of extinction coefficients for the purpose of the evaluation of sun-screens has been employed only once to my knowledge, and was briefly reported by Friedlaender *et al* (1948).

### MATERIALS AND METHOD.

The following substances were used : aesculin, tannic acid, para-aminobenzoic acid, salol, pyribenzamine, antipyrine, sulphanilamide, nicotinic acid and resorcin. Various concentrations in appropriate solutions were investigated

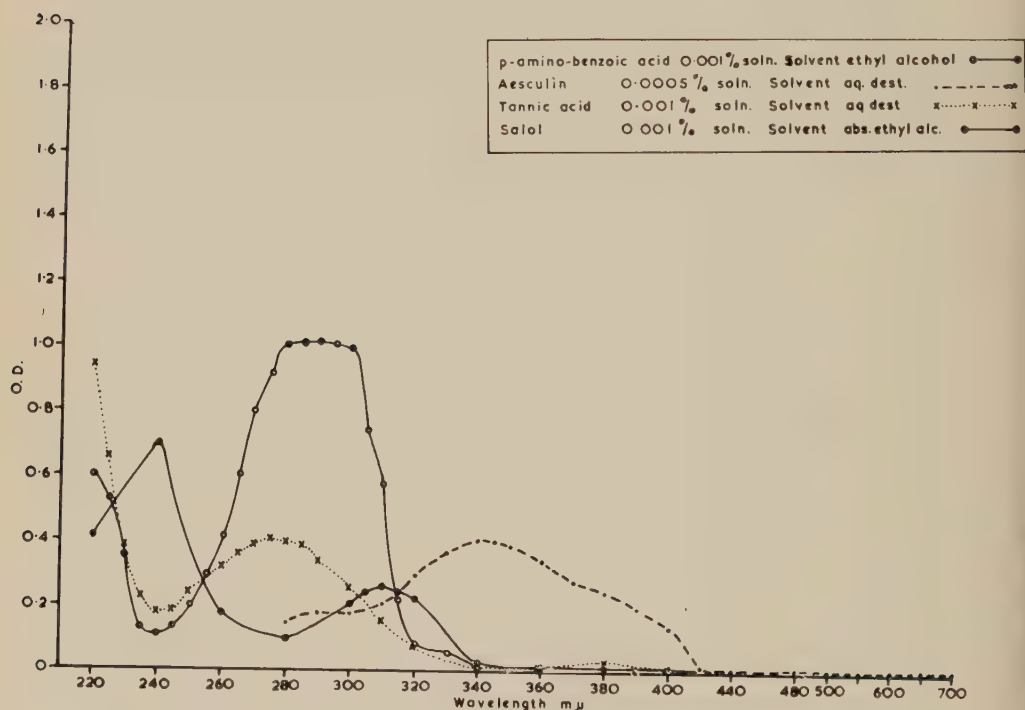


FIG. 1.—Absorption spectra of *p*-amino benzoic acid, aesculin, tannic acid and salol. O.D. represents optical density.

by means of a Cambridge Unipivot spectrophotometer and the results obtained expressed as optical densities plotted against wavelengths (Figs. 1 and 2). The substance under investigation was usually diluted to 0.001–0.005% and distilled water used whenever possible as diluent. The quartz cell in which the material was placed was 1 cm. square. A quartz mercury lamp vapour was

used for wavelengths shorter than  $4000\text{\AA}$  and a hydrogen arc for those of  $4000\text{\AA}$  and longer. For comparison, the measurements obtained were reduced by using Beer's equation :

$$E = \frac{1}{d} \times \log \frac{I}{I_0}$$

where  $\log \frac{I}{I_0}$  represents the density of the solution,  $I$  the intensity of incident light (always considered to be 100%), and  $I_0$  the intensity of the transmitted light ;  $d$  is the thickness of the solution in cm. and  $C$  the concentration per

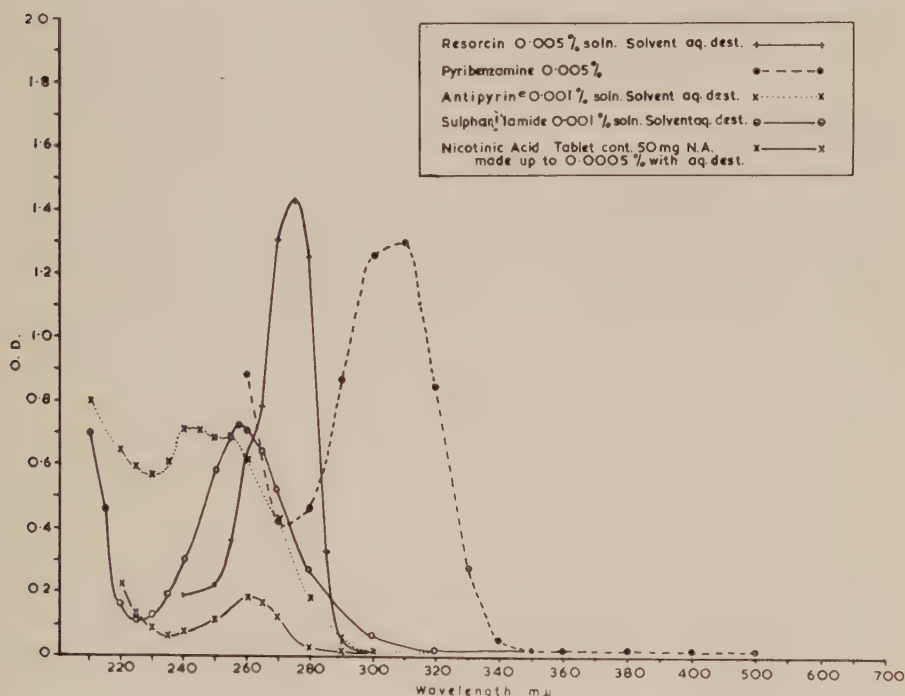


FIG. 2.—Absorption spectra of resorcin, pyribenzamine, antipyrine, sulphanilamide and nicotinic acid. O.D. represents optical density.

cent (weight/volume).  $E$  is designated the extinction coefficient. If  $E$  is known, by using the same equation the intensity of the rays transmitted by various concentrations of sunscreens can be determined. The equation holds in a large number of cases over considerable ranges of concentration. In such a way the comparative absorptive capacity of various sunscreens can best be seen. As sunscreens are not all used in the same concentrations their real protective capacity when used in different concentrations can only be surmised from the absorption curve alone.



Extinction coefficients for wavelengths of 2900Å–5000Å were calculated (Table I). The percentage of transmission at the same wavelengths was worked out for the concentrations in which these substances are usually used in sun protecting preparations and for layers 0.05 mm. thick, this being the usual thickness of an ointment when spread normally on the skin (Table II).

#### DISCUSSION.

Previous investigators have used a spectrophotometer or an artificial source of light; in the latter case the rays of the lamp were projected on to the subject's back which was previously covered with the sunscreens in question. In all except one publication (Lorentzen, 1955), where a spectrophotometer was used, the results were not given as the absorption curves of various sunscreens but only as a linear representation. From such a line, the optical density of a sunscreen at different wavelengths cannot be seen. With the second method there are two possible sources of error, the sunscreens and the lamp.

The film of the sunscreen, however much care is taken, cannot be spread evenly over the test site; when two or more sunscreens are tested simultaneously, the different sensitivity to light of various parts of the body must be taken into account as well, when evaluating relative protective capacity. In order to overcome this obstacle, the method advised by Koch (1947) is of value. A visual estimation of erythema is highly inaccurate, for the eye is a poor judge of absolute brightness of colour.

The spectral intensity of the different wavelengths of light from a lamp does not correspond to that of sunlight. The erythema producing wavelengths begin approximately at 2300Å and produce a stronger erythema at 2600Å. They have a minimum effect at 2800Å and another increase at 3000Å, with a steep fall towards longer wavelengths. Therefore an erythema produced with an artificial light source cannot be the only criterion for the assessment of the protective capacity of an application against sunlight, as erythema can be produced either by ultra-violet C rays which are not included in the sun's spectrum, or ultra-violet B rays which are.

The amount of irradiation reaching the skin surface depends on the angle of incidence and even neighbouring areas will not receive exactly equal intensities of radiation (Henschke, 1948) which is another snag when this method is used.

An ideal sunscreen should be one which absorbs the majority of the rays which cause or aggravate a dermatosis. In most dermatoses it is the ultra-violet part of the spectrum which is responsible. As the same rays produce erythema in all individuals, sunscreens should be also used under some special circumstances such as expeditions or abnormally long exposures. Light sensitivity in polymorphic light eruptions is limited to the ultra-violet spectrum,



mainly ultra-violet B but partly ultra-violet A. Ultra-violet C is not taken into consideration here as it is not included in that part of the sun's spectrum which reaches the earth. We can assume that in skin diseases, the lesions of which can be produced by sunlight and are based on a Koebner phenomenon mechanism, ultra-violet rays possessing the greatest energy are responsible for such an effect. We can expect, therefore, that all sunscreens absorbing in this part of the spectrum should produce benefit. With urticaria solare which responds to wavelengths of the blue-violet spectrum (4000Å–5000Å) an attempt should be made at prescribing a sunscreen the absorption of which lies mainly in this band; a sunscreen with a good absorption at shorter wavelengths does not necessarily have a good absorption at the above wavelengths and *vice versa*. The exact knowledge of the maximum and minimum absorption of a sunscreen has, therefore, a wide application. Theoretically, by exposing the skin to ultra-violet A rays which produce pigment darkening and at the same time protecting from ultra-violet B rays, it could be sun-tanned without the risk of an unnecessary early erythema produced by ultra-violet B. A sunscreen which fulfils these two requirements has, however, not yet been found.

In a sunscreen ointment, the base absorbs certain wavelengths. This fact has to be taken into consideration when evaluating the power of absorption of a sunscreening ointment.

From Table II it follows that aesculin in 10% or 5% concentration is without doubt the best sunscreen in the group investigated. Its high absorption in the band 3000Å–4000Å makes its use particularly appropriate for urticaria solare produced by these wavelengths. Its relatively high price however, represents a disadvantage. Salol used in 10% concentration seems to be the best protective substance apart from aesculin for ultra-violet B and shorter rays of ultra-violet A. Satisfactory experimental results with salol have been reported by Sharlitt (1935) and Luckiesh (1946).

Para-aminobenzoic acid comes after the former two in order of effectiveness. It gives protection when used either in 15% or 10% concentration. It has been praised by Beal (1948) and Rothman and Hennigsen (1947) proved its protective power in normal subjects. In France, however, it is not popular because of its capacity to cause eczematous contact sensitization as well as cross sensitivity with other substances possessing a para-aminobenzene group (Jausion *et al.*, 1950).

The absorption of pyribenzamine in 5% and 10% concentration at wavelengths up to 3400Å does not differ much from those mentioned above at longer wavelengths it is, however, considerably smaller, which is important if a patient is sensitive to wavelengths of 3400Å and longer. Pyribenzamine represents the antihistaminic drug most used for sunscreening purposes. It has to be pointed out that its sunscreening action is not based on its antihistaminic properties; benadryl, though an antihistaminic, is far less potent as a sunscreening sub-



stance (Baer *et al.*, 1948). Pyribenzamine, owing to its antipruritic action, is very useful in light sensitivity cases, which are always associated with a certain degree of pruritus (Feinberg and Bernstein, 1947).

Tannic acid used in 10% or 5% concentration also offers very good protection. It can however, produce a feeling of stiffness of the skin. It has been recommended by Meyer and Amster (1925) and Polano (1952) found a cream of the O/W type containing 5–10% of tannic acid to be highly efficacious. The threshold of erythema was four to eight times higher than when the base alone was used. It is interesting that when tannic acid in a W/O emulsion was used, it did not give any protection.

Sulphanilamide, because of its high sensitizing capacity, is rarely used nowadays. As a sunscreen, it comes after the above mentioned substances in order of efficacy.

Antipyrine, praised as a sunscreen by Quiroga *et al.* (1948) was found in my experiments to be inferior to the substances discussed. In 4% and 8% concentration, in which it was recommended, it transmitted wavelengths of 3000Å and longer.

Both nicotinic acid in 4% and 8% concentration and resorcin in 2% concentration, which sometimes have been used as sunscreens, are very poor absorbers of sunlight.

The topical use of nicotinic acid was recommended by Jausion *et al.* (1950) who believed its effect to be photochemical and due to the penetration of nicotinic acid into the skin. It might be, therefore, that nicotinic acid exerts a stronger protective action than that indicated by the physical measurements.

From these investigations it follows that some of the sunscreens discussed above can be used for patients sensitive to ultra-violet B and A. For urticaria solare, which is produced by wavelengths of 4000Å–5000Å, no sunscreen apart from aesculin is capable of absorbing sufficient sunlight of this band to afford protection.

#### SUMMARY.

The absorption spectra of some sunscreens have been measured and the transmission through them of wavelengths of 2900Å–5000Å have been calculated, using concentrations of them customary in ointments.

The least transmission was found with aesculin, followed by salol, pyribenzamine, para-aminobenzoic acid, tannic acid, sulphanilamide, antipyrine, nicotinic acid and resorcin, in order of increasing transmission.

This work was carried out in the Department of Dermatology, Addenbrooke's Hospital, Cambridge, under the supervision of Dr. A. J. Rook, during the tenure of a Trinity College bursary to Cambridge University.

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## DIHYDROXYACETONE.

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DURING recent months, preparations designed to "tan" the skin have reached the cosmetic market. They are claimed to produce a pigmentation of the skin which is indistinguishable from that following exposure to sunlight. The active agent in the solutions is dihydroxyacetone (D.H.A.). The substance is stated to be a carbohydrate classified as a monosaccharide. As a white crystalline powder it is soluble in one part of water and fifteen parts of alcohol. The exact chemical nature of the colour reaction is not certain but it is probable that a compound is formed by one of the hydroxyl radicals of D.H.A. with amino-acids in the superficial layers of keratin, followed by complex polymerization resulting in the production of a brown pigment. This pigment is certainly not melanin.

### INVESTIGATION.

The following experimental formula has been tested :

|                    |   |   |   |     |
|--------------------|---|---|---|-----|
| D.H.A.             | . | . | . | 2.5 |
| Glycerin           | . | . | . | 2.5 |
| Methylated Spirits | . | . | . | 33  |
| Water to           | . | . | . | 100 |

Painting of human skin with this solution is followed in six to ten hours by a light brown pigmentation. If repeated applications at hourly intervals are made, the depth of colour is increased up to a light negroid tint. The colour cannot be removed with active cleansing agents or fat solvents or by mechanical superficial abrasion. It gradually disappears during the course of five to eight days.

Application of the above solution to thirty-two normal and ten eczematous skins produced the phenomenon described in the preceding paragraph. In no case was there any evidence of irritation or complaint of local discomfort. There was considerable variation in the depth of tint induced by a single application. Frequent washing of the painted areas (after the colour had developed) slightly lessened the duration of pigmentation. Horny skin such as that found on the volar aspect of the finger developed more persistent browning.

The preparation does not diminish the response to U.V.R. Comparative tests of painted and unpainted skin showed equal erythema and oedema, though the colour of the former was masked. Recently excised human mammary skin did not appear to develop pigment even after repeated applications, but soaking keratinized scales from a verruca turned them deep brown.

The substance might be expected to provide cosmetic relief in vitiligo. A number of sufferers from this condition were painted with D.H.A. and the areas of leucoderma developed reactions similar to those of the unaffected skin. Each case, however, required a test on a basis of trial and error, since it was found that the number of applications and the intervals between them necessary to give a matched colour varied



considerably from individual to individual. Also it was found that unless the painting was carried out carefully the cosmetic result was imperfect, previously pigmented skin on the periphery of the vitiliginous area developing a yet darker colour, as might be expected.

For the treatment of vitiligo, several modifications in the vehicle employed to carry the D.H.A. would seem advisable. Perhaps a cream of comparatively low wetting capacity with an added tracer colour, washable after one hour, would render accurate applications easier.

The free use of this substance on face or limbs by those seeking a rapidly achieved "healthy" appearance may be accompanied by certain practical risks—for example it is most difficult to induce even tinting over a large area. If inexpert, the user may induce a streaked and bizarre pattern which may detain him or her in the home for a week until normality has been regained. This risk is greater because of the delay between application of solution and development of colour. Thoughtless purchasers may consider that when the skin appears deeply tinted exposure to sunshine is safe. Risks of severe reactions to over-exposure are to be envisaged.

It is hoped that this preliminary communication will stimulate interest in the action and use of D.H.A.

The writer is indebted to Messrs. Pfizer Ltd., for the chemical references.

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## BOOK REVIEWS.

## EFFECTS OF ULTRA-VIOLET RADIATION.\*

For many years the author has been deeply interested in the effects of light on the skin and has carried out an immense amount of original research on the subject. His findings and his views, published in a book and a large number of papers, are probably the first source to which others turn when seeking knowledge. He has done, perhaps, more than any other to place the study of this difficult matter on a scientific basis and to insist on the most careful interpretation of results.

It is therefore of the utmost value to have, collected in one medium-sized book, the most recent views of so notable a worker. The subject is dealt with broadly and necessarily many chapters are concerned with such related matters as the effects of ultra-violet radiation on living organisms, the curious phenomenon of photo-recovery, cell division and reduplication, the mechanism of inheritance and kindred subjects. There is a stimulating chapter of speculation on the fundamental nature of cancer and the manner in which a cancer cell differs from a normal one, and here the author puts forward his own original ideas supported by careful reasoning. The reading is not always easy for those who are not mathematically inclined and probably most dermatologists will be tempted to read first the excellent account of sunburn of the human skin. To the specialized worker, the accounts of experiments and the carefully recorded results are of the greatest importance.

To sum up, one might say that this is a book of exceptional interest to a small number, but it is probably too remote from ordinary clinical experience to appeal to the average dermatologist. The book is well produced, contains a few good photographs grouped in the centre, and many diagrams.

A. D. P.

## AN INTERNATIONAL REVIEW.†

THIS first volume in a new series was conceived as a *Festschrift* for the late Prof. W. Lutz but, unhappily, had to be dedicated to his memory. Twenty-one articles, mostly in German, cover nine topics: physiology of skin, autonomic nervous system, allergy, mycology, vasculitis, reticulosis, porphyrins, radiology and new drugs. The contributors are mostly from University departments and write on subjects in which they are specially interested and on which they may have worked. These reviews would be most valuable to younger dermatologists requiring surveys in fields they may hope to make their own, and to those coming to dermatology with a broad scientific background, but might prove rather heavy going for the clinician. The volume is well produced, a credit to editor, contributors and publisher and shows (as did MacKenna's *Modern Trends*) that dermatology is a lively and expanding branch of science. Leonhardi and Steigleder marshal extensive new knowledge on bio- and histochemistry of skin enzymes. The Basle school write on the autonomic nervous system, contact dermatitis and antibodies, serology of systemic L.E. (P. Miescher) and porphyrins (Schuppli). Radioactive isotopes and their new applications to dermatology are covered. Results of treatment in pemphigus vulgaris and erythematosis since the cortisone era (from Jerusalem) would interest clinicians.

M. F.

\**Carcinogenesis by ultra-violet light*. HAROLD F. BLUM (1959). Princeton, New Jersey: Princeton University Press. Pp. 340. 60 illustrations. Price 52s.

† *Current Problems in Dermatology*. Vol. 1. R. SCHUPPLI, Editor (1959). Basle, New York: S. Karger. Pp. 522. 98 Illus. Price 48 Swiss Francs.



## CURRENT LITERATURE

**TRIAMCINOLONE TREATMENT OF PSORIASIS.** O. LOFFERER and R. PLASUN. (1959) *Derm. Wschr.*, 140, 750.

Twenty-seven patients were treated, mostly severe and resistant cases. Initial, then daily dose was 16-32 mg. Other corticosteroids were almost uniformly unsuccessful. The authors suggest prolonged treatment with a daily maintenance dose of 4-8 mg. Residual lesions can then be treated in the usual manner.

Side effects after a few months were rounding or definite mooning of face, and insomnia in one patient. The treatment is recommended during severe episodes and in exudative cases and where large plaques predominate as well as in pustular psoriasis. Arthropathy improved as well.

J. M.

**IRRADIATION SARCOMA AND CARCINOMA AFTER X-RAY THERAPY FOR LUPUS VULGARIS.** A. WAGNER and W. PILCHOWSKI. (1959) *Derm. Wschr.*, 140, 766.

A man aged 46 suffered from lupus vulgaris in childhood. X-ray therapy to lower parts of face was repeatedly given. A squamous cell epithelioma developed 30 years later on the skin which showed evidence of radio-dermatitis. Further x-ray therapy failed to eradicate the carcinoma and eighteen months later a fibrosarcoma was diagnosed histologically. One feels that radiotherapy would not be employed in this country on a skin damaged by irradiation and a past history of lupus vulgaris.

J. M.

**TREATMENT OF TELANGIECTASIA.** A. W. THÖNE. (1959) *Derm. Wschr.*, 140, 789.

Seventy cases were treated and carefully followed up. The only treatment recommended is electro-cautery using a fine point. Smaller lesions to be treated without local anaesthetic (spider naevi)—otherwise a certain amount of scarring is inevitable. Larger "papular" lesions need more thorough treatment and local anaesthesia has to be employed. One-third of the cases need repeated treatment. Naevoid macular lesions and telangiectatic "rami" do not respond.

J. M.

**CLINICAL AND HISTOLOGICAL RELATIONSHIP OF SOME FORMS OF GUTTATE PARAPSORIASIS AND ALLERGIC VASCULITIS (RUITER).** H. KRÜGER and H. J. WEISE. (1959) *Derm. Wschr.*, 140, 813.

After clinical and histological evaluation of 3 cases following the classification of Gougerot and Ruiter, the authors feel that pityriasis lichenoides chronica and the papulo-necrotic type of allergic vasculitis are closely related.

J. M.

**ATOPIC DERMATITIS: AN HYPOTHESIS.** FRANK A. SIMON. (1959) *Acta Allergol.*, 13, 383.

The cause of this disease may be found in the skin itself, probably associated with sebaceous glands and hair follicles. Human dander and the epidermis of the general body surface contain an allergen to which 75% of atopics give positive patch, scratch or intradermal tests.

H. T. H. W.

**THE NATURE OF THE ECZEMATOGENIC SUBSTANCE IN MICROBIAL ECZEMA.** JOHANNES MEYER-ROHN and BERNWARD ROHDE. (1959) *Acta Allergol.*, 13, 389.

Scratch tests with bacterial fractions from cases with microbial eczema were carried out on eczematous subjects and normal controls. The results were indeterminate and suggest that bacterial bodies have no significant eczematogenic properties.

H. T. H. W.

**BESNIER'S PRURIGO.** R. ARON-BRUNETIERE. (1959) *Acta Allergol.*, 13, 395.

Acetylcholine improves most cases of prurigo and senile pruritus but tends to aggravate microbial eczema and contact dermatitis.

H. T. H. W.